REMARKS

Claims 12-52 are pending. Claims 20-25 have been previously withdrawn from consideration. Claims 1-11 have been cancelled. The Examiner indicated, during the October 24, 2003 interview that claims 12 and 26 are allowable in their current form. Dependent claims 18 and 29 have been amended to remove certain objections that were raised during the interview. New claims 32-52 have been added. Support for the new claims can be found throughout the specification, or the claims as originally filed. No new matter has been added

Amendment or cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to more particularly point out and distinctly claim the invention to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

The Invention

The claimed invention generally relates to methods for altering expression of a glutamic acid decarboxylase (GAD) in a region of the brain. This is accomplished by identifying a target site in the central nervous system that requires modification and delivering a vector that comprises a nucleic acid sequence encoding glutamic acid decarboxylase (GAD) to a target site of the central nervous system (e.g., a region of the brain), to alter expression of GAD in the region of the brain.

More specifically, the present application also discloses and claims a method of treating a disease by delivering a vector that comprises a nucleic acid sequence encoding glutamic acid decarboxylase (GAD) to target cells of the central nervous system (e.g., a region of the brain), to treat or reduce a neurodegenerative disease. Applicants have discovered that increased levels of GAD can ameliorate certain central nervous system (CNS) diseases, and that gene therapy can be used effectively to increase GAD in the central nervous system.

Even more specifically the invention demonstrates the principal that expression of GAD in a region of the brain alleviates the symptoms of Parkinson's disease.

Claim Objections and Rejections

The Examiner, in her October 24, 2003 interview with applicants, agreed that claims 12 and 26 are allowable in their current form. Dependent claims 13-19 (dependent on claim 12) and 27-31 (dependent on claim 26) were also discussed. The Examiner objected to dependent claims 18 and 29. Those claims have been amended to remove the Examiner's stated objections. Claims 1-11 have been cancelled. Claims 12-19 and 26-31 are therefore in condition for allowance in their current form and should be allowed.

New Claims

New claims 32-51 are presented. Claims 32 and 44 are independent.

Claim 32 recites a method for altering expression of glutamic acid decarboxylase (GAD) in a region of the central nervous system (CNS) of a subject by identifying a target site in the CNS that requires modification, delivering a vector comprising a sequence encoding GAD to the CNS target site and expressing GAD in the target site.

Claim 44 recites the identical method of claim 32, wherein the subject has a disorder which causes morphological and/or functional abnormality of a neural cell or population of neural cells.

Applicants hereby submit the Rule 132 Declaration of Dr. Michael Kaplitt (hereinafter "Kaplitt Decl.") with the evidence discussed in the interview regarding the new claims.

Applicants have shown that GAD gene transfer into glutamatergic excitatory neurons leads to an inhibitory bias with altered network activity. This phenotypic shift provides strong neuroprotection and demonstrates there is plasticity between excitatory and inhibitory neurotransmission in the mammalian brain that results in a therapeutic effect, in particular the alleviation of symptoms of Parkinson's disease (Kaplitt Decl. para. 5-6).

The same inventive concept of delivering GAD to a region of the central nervous system, can be applied to any CNS disease in which increasing GABA production is desirable (Kaplitt Decl. para. 7). Applicants have used the method of the invention, to reduce the symptoms of epilepsy, by delivering GAD to a region of the brain involved in epilepsy, e.g., the hippocampus. (Kaplitt Decl. para. 8-10). Other groups have used the vectors and/or methods of the application to target regions of the brain to address such other conditions such as metabolic disorders. (Kaplitt Decl. para. 11-12) and chronic pain (Kaplitt Decl. para 13-14).

The teaching of the application is not limited to the delivery methods of the examples. Other vectors, for example, may be used to target the CNS and alter GAD expression (Kaplitt Decl. para. 13-14)

Finally, it is obvious that GAD can be targeted specifically to different regions of the brain including the hippocampus (Kaplitt Decl. para. 8), the lateral nucleus of the hypothalamus (Kaplitt Decl. para. 12), the rostral agranular insular cortex (RAIC) (Kaplitt Decl. para. 14) and even the visual cortex (Kaplitt Decl. para. 16).

Thus one of ordinary skill in the art, would be able to use the application's disclosure, in addition to the knowledge available in the art, to apply the invention to alter expression of glutamic acid decarboxylase (GAD) in a selected region of the CNS.

In summary, the disclosure in the application, in combination with the knowledge available in the art, would enable one skilled in the art to perform the full scope of the claimed invention without undue experimentation.

Conclusion

For all the reasons above, reconsideration and allowance are requested. The Examiner is urged to call the undersigned at the telephone number indicated below so that any remaining issues can be discussed.

Respectfully submitted,
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